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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/816,688	03/22/2001	Katherine A. High	018743-0278737	5212

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PILLSBURY WINTHROP SHAW PITTMAN LLP
ATTENTION: DOCKETING DEPARTMENT
P.O BOX 10500
McLean, VA 22102

EXAMINER	
WHITEMAN, BRIAN A	
ART UNIT	**PAPER NUMBER**
1635	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/24/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/816,688	HIGH ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 13-63* is/are pending in the application.

4a) Of the above claim(s) *33,36-40,42-63* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,13-32,34,35,41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 2, and 13-63 are pending.

Election/Restrictions

Claims 33, 36-40, 42-63 and the polypeptide in claim 34 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention and adenovirus, parvovirus, papilloma virus, reovirus, rotavirus and herpes virus in claim 31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 4/7/06.

Claim Objections

Claim 34 is objected to because of the following informalities: the claim reads on a non-elected invention. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 13-25, 29, 30, 32, 34, 35, and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wolf (US 5,795,863) taken with Nicolaisen (US 5,580,560). Wolf teaches:

> A slow release form of Factor X, comprising a single chain precursor polypeptide comprising the light and heavy chain of Factor X in which at least a portion of the native activation peptide sequence has been deleted and a proteolytic cleavage site has been inserted between the C-terminus of said light chain and the N-terminus of said heavy chain, said polypeptide being convertible to Factor Xai by proteolysis and capable of competing with native Factor Xa in the formation of a prothrombinase complex, and said

light chain or said heavy chain being modified from its native amino acid sequence so that said Factor Xai lacks protease activity when incorporated into said prothrombinase complex, wherein said proteolytic cleavage site has the sequence RKRRKR. See columns 31-32.

However, Wolf does not specifically teach Factor VII or Factor IX having the proteolytic cleavage site.

However, at the time the invention was made, Nicolaisen teaches that the cDNA coding for Factor VII has been characterized (columns 1-2). The analysis teaches that cleavage of a single peptide bond between arginine 152 and isoleucine 153 converts Factor VII to Factor VIIa. "Factor VIIa has been found to be a protein susceptible to proteolytic cleavage giving rise to a number of degradation products without clotting activity." See column 2. "A need exists in the art for factor VIIa preparations which are stable during production, purification and storage even at high concentrations, and which furthermore have a longer half life and slower clearance from the blood than the native or recombinant factor VIIa." See column 3. Nicolaisen teaches producing the protein in a cell using an expression vector comprising the nucleic acid (columns 5-6 and 10).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Wolf taken with Nicolaisen, namely to produce a composition comprising a nucleic acid encoding a modified Factor VII having the proteolytic cleavage site as set forth in SEQ ID NO: 1. One of ordinary skill in the art would have been motivated to combine the teaching to produce a slow release form of Factor VII.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Wolf taken with Nicolaisen, namely to produce a nucleic acid encoding factor VII analogue with a modified cleavage site between arginine 152 and isoleucine 153. One of ordinary skill in the art would have been motivated to combine the teaching because the active cleavage site of Factor VII is between these two amino acids.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Wolf taken with Nicolaisen, namely to produce a vector comprising the nucleic acid encoding factor VII analogue with a modified cleavage site. One of ordinary skill in the art would have been motivated to combine the teaching to express the nucleic acid in a cell.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments, see pages 8-12, filed 10/26/06, with respect to the rejection(s) of claim(s) 1, 3, 4, 13, 14, 18-20, 24, and 28 under 103(a) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of the newly discovered reference(s).

With respect to applicant's argument that the term "instructions confer patentable weight when the printed matter is functional (see In re Gulack), the argument is not found persuasive because the printed matter is not functional and does not interrelate to the kit. Here, addition of a new set of instructions into a known kit does not interrelated with the kit in the same way as the numbers interrelated with the band as discussed in Gulack.

Claims 1, 24, and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wolf taken with Nicolaisen as applied to claims 1, 2, 13-25, 29, 30, 32, 34, 35, and 41 above, and further in view of Amalfitano et al. (US 6328958).

Wolf taken with Nicolaisen do not specifically teach using an EF-1-alpha promoter in the composition.

However, at the time the invention was made, Amalfitano teaches a heterologous nucleotide sequence (e.g., clotting factor) operatively associated with a cytomegalovirus (CMV) major immediate-early promoter, an albumin promoter, an Elongation Factor 1-.alpha. (EF1-.alpha.) promoter, a P.gamma.K promoter, a MFG promoter, or a Rous sarcoma virus promoter. See columns 19-20.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Wolf taken with Nicolaisen in further view of Amalfitano, namely to produce the composition comprising an EF1-alpha promoter. One of ordinary skill in the art would have been motivated to combine the teaching to sufficiently express Factor VII in a cell.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 1, 24, 26, and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wolf taken with Nicolaisen as applied to claims 1, 2, 13-25, 29, 30, 32, 34, 35, and 41 above, and further in view of Kochanek (US 5,981,225).

Wolf taken with Nicolaisen do not specifically teach using a skeletal muscle actin or muscle creatine kinase (MCK) promoter in the composition.

However, at the time the invention was made, the use of the MCK promoter will lead to tissue specific expression of a foreign gene (column 13).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Wolf taken with Nicolaisen in further view of Kochanek, namely to produce the composition comprising a skeletal muscle actin or muscle creatine kinase promoter. One of ordinary skill in the art would have been motivated to combine the teaching to selectively express Factor VII in a desired cell.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 1 and 29-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wolf taken with Nicolaisen as applied to claims 1, 2, 13-25, 29, 30, 32, 34, 35, and 41 above, and further in view of Kay et al. (US 5,980,886).

Wolf taken with Nicolaisen do not specifically teach using a viral vector.

However, at the time the invention was made, adenoviral and retroviral vectors were well known to one of ordinary skill in the art for expressing a protein in a liver cell as exemplified by Kay (column 2).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Wolf taken with Nicolaisen in further view of Kay, namely to produce the composition comprising a viral vector selected from an

adenovirus and retrovirus. One of ordinary skill in the art would have been motivated to combine the teaching to sufficiently express Factor VII in a liver cell.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Douglas Schultz, PhD, SPE – Art Unit 1635, can be reached at (571) 272-0763.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

D. W